UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/531,969	03/21/2000	Jan Geliebter	96700/596	6902

7590 02/21/2002

Craig J Arnold Esq
Amster Rothstein & Ebenstein
90 Park Avenue
New York, NY 10016

EXAMINER	
PARAS JR, PETER	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/531,969	GELIEBTER ET AL.	
	Examiner	Art Unit	
	Peter Paras	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9,20 and 37-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9,20 and 37-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's amendment filed on November 6, 2001 has been entered. Claims 1 and 9 have been amended. Claims 6-8, 10-19, and 21-36 have been cancelled. New claims 37-49 have been added. Claims 1-5, 9, 20, and 37-49 are pending and are under current consideration.

Terminal Disclaimer

The terminal disclaimer filed on 11/6/01 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 6,150,338 and 6,239,177 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 20, 37-38, and 45 as originally filed, amended, or newly added are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record advanced on pages 2-4 of the Office action mailed on 6/6/01.

Applicants have amended the originally filed claims to read methods of regulating smooth muscle tone by introduction of a nucleic acid sequence, encoding a potassium channel protein, into smooth muscle cells such that the nucleic acid sequence is expressed and smooth muscle tone is regulated.

In response, the Examiner maintains that while the specification has described methods of regulating penile and bladder smooth muscle tone with a nucleic acid sequence encoding Maxi-K and a method of regulating penile smooth muscle tone with a nucleic acid sequence encoding Kir6.2, the specification has not described regulation of smooth muscle tone by introduction of any other nucleic acid sequences encoding potassium channel proteins. The specification fails to describe other nucleic acid sequences, encoding potassium channel proteins, which when introduced and expressed into smooth muscle cells result in regulation of smooth muscle tone. See page 3 of the Office action mailed on 6/6/01. The state of the art is such that *in vivo* expression of nucleic acid molecules encoding potassium channel proteins other than Maxi-K or Kir6.2, which resulted in regulation of smooth muscle tone were not known. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicant's effective filing date. Possession may be shown by reduction to practice. However, the instant specification has not reduced to practice methods of regulating smooth muscle tone with nucleic acid sequences encoding potassium channel proteins other Maxi-k or Kir6.2 K_{ATP} subunit; such methods lack a written description. The specification has failed to describe what

other genes fall into the genus of genes that encode potassium channel proteins. It was unknown as of Applicant's effective filing date that any of these genes would have the properties of regulating smooth muscle tone. The skilled artisan cannot envision the method steps, including the use of nucleic acid sequences that encode all other potassium channel proteins in such method steps, necessary to practice the claimed invention, regardless of the complexity or simplicity of the method, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method.

Accordingly, the previous rejection is maintained for the reasons of record.

Claims 1-5, 9, 20, and 37-49 as originally filed, amended, or newly added are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treatment of bladder dysfunction or treatment of erectile dysfunction caused by heightened contractility of smooth muscle cells by direct injection of a nucleotide sequence encoding Maxi-K into bladder or penile smooth muscle cells, wherein expression of Maxi-K regulates smooth muscle tone by resulting in less heightened contractility of penile or bladder smooth muscle cells; and a method of treatment of erectile dysfunction caused by heightened contractility of smooth muscle cells by direct injection of a nucleotide sequence encoding the Kir6.2 K_{ATP} subunit into penile smooth muscle cells, wherein expression of Kir6.2 regulates smooth muscle tone by resulting in less heightened contractility of penile smooth muscle cells, does not reasonably provide enablement for all other methods of regulating smooth muscle tone.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record advanced on pages 5-11 of the Office action mailed on 6/6/01.

Applicants assert that the specification provides evidence that a DNA sequence encoding a potassium channel protein, either Maxi-K or K_{ATP}, can regulate smooth muscle tone, either in penis or bladder. Applicants submit that, based upon these results, the skilled artisan would have a reasonable expectation that a DNA sequence encoding other potassium channel proteins would have a similar regulatory effect in other types of smooth muscle. See the amendment on pages 4-5.

In response, the Examiner maintains that the claims as written are only enabled for the scope set forth above. The claims as written are broad with respect to nucleic acid sequences encoding potassium channel proteins, types of smooth muscle cells, mode of administration of DNA sequences, and effect of expression of any nucleic acid sequence in smooth muscle cells. The claims as they are broadly written are not enabled. The enabled scope is specific with respect DNA sequences, effects of expression of DNA sequences, and smooth muscle cell types.

The working examples provided by the instant specification are only directed to the use of nucleic acid sequences encoding maxi-K or Kir6.2 for regulation of smooth muscle cells of the bladder or penis resulting in less heightened contractility. The art of gene therapy at the time the claimed invention was filed was unpredictable with respect to expression of a heterologous nucleic acid sequence and a resulting therapeutic effect.

See Eck and Wilson on pages 7-8 of the Office action mailed on 6/6/01. The claims as written do not require any particular effect resulting from expression of maxi-K or Kir6.2. It is unpredictable if expression of maxi-k or Kir6.2 can result in treatment of other types of penile or bladder smooth muscle dysfunction, for example treatment of dysfunctions that require heightened contractility of smooth muscle. There is no evidence of record that suggests that expression of maxi-K or Kir6.2 can result in heightened contractility of smooth muscle. Further, the claims allowed in related patents 6,271,211, 6,150,338 and 6,239,177 are all directed to regulation of smooth muscle tone resulting in less heightened contractility. As such the evidence of record has not provided a correlation between expression of maxi-K or Kir6.2 and treatment of other types of smooth muscle dysfunction. Next, the instant specification has not provided any guidance or relevant teachings that suggest expression of maxi-K or Kir6.2 can regulate smooth muscle tone in smooth muscle cell types other than bladder or penile. Moreover, it is unpredictable if expression of any nucleic acid sequences encoding potassium channel proteins can regulate the tone of any smooth muscle for the treatment of any type of dysfunction, including those recited in claim 20. The instant specification has not provided any relevant teachings, guidance, or working examples that correlate expression of any potassium channel protein with regulation of tone of any smooth muscle type for the treatment of any dysfunction. Given, the unpredictable nature of the art of gene therapy and the lack of guidance provided by the instant specification the skilled artisan would not have had a reasonable expectation of success in attempts to regulate any smooth muscle cell with any nucleic acid sequence encoding a potassium channel protein.

Finally, with respect to gene delivery and cell targeting the instant specification has only provided guidance with respect to direct injection of DNA sequences into smooth muscle cells of the bladder and penis. It is maintained that all other modes of gene delivery and cell targeting are not enabled by the instant specification. It is further maintained that vector targeting to specific cells is unpredictable and inefficient. See Miller, Deonarain, Verma, and Crystal on pages 9-10 of the Office action mailed on 6/6/01. The evidence of record fails to correlate other modes of delivery of nucleotide sequences encoding potassium channels encompassed by the instant claims with targeting of any smooth muscle cells. The guidance and working examples provided by the instant specification are only directed to direct injection of a DNA sequence into a smooth muscle cell. Further, the allowed claims of related patents 6,271,211, 6,150,338 and 6,239,177 are only directed to direct injection of a DNA sequence into a smooth muscle cell.

Accordingly, the rejection is maintained for the reasons of record.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 7-19, 21-27, and 30-34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn as the

rejected claims have been cancelled with the exception of claim 9, the dependency of which has been amended to claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The previous rejection of claims 21-25, 27-33, and 35-36 under 35 U.S.C. 102(e) as being anticipated by Kaczorowski is withdrawn as the claims have been cancelled.

The previous rejection of claims 21-23, 27-31, and 35-36 under 35 U.S.C. 102(e) as being anticipated by Kalecko is withdrawn as the claims have been cancelled.

The previous rejection of claims 21, 25-27, 28 and 33-34 under 35 U.S.C. 102(e) as being anticipated by Yoshitaka is withdrawn as the claims have been cancelled.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The previous double patenting rejections over US 6,150,338 and US 6,239,177 are withdrawn as Applicants have filed a terminal disclaimer over the patents.

The following are new grounds of double patenting rejections:

Claims 1-5, 9, 20, 37, 40, 42, 45, and 47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,271,211. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to

methods of regulating smooth muscle tone, wherein a nucleic acid sequence encoding a potassium channel protein is introduced into smooth muscle cells, particularly when the nucleic acid sequence encodes Kir6.2 and is introduced into penile smooth muscle to treat erectile dysfunction.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Patsy Zimmerman whose telephone number is (703) 305-2758.

Scott D Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Peter Paras, Jr.

Art Unit 1632